

Appln No.: 08/822,186

Amendment dated June 4, 2004

In Response to Examiner's Office Action dated March 4, 2004

REMARKS

Claims 1-6, 8, 9, 11-25, 31-33 and 35-38 are pending in this application. Claims 7, 10, 26-30 and 34 are canceled. Claims 37 and 38 are added. Claims 6, 9 and 14 are withdrawn as being drawn to nonelected species. Upon allowance of the generic claim, applicant will request rejoinder of claims 6, 9 and 14.

Applicants have amended claims 1, 32 and 35 to recite a "bone morphogenetic protein" rather than "osteogenic protein." Support for this amendment is provided, e.g., on page 1, lines 10-13; and page 5, lines 11-14 of the specification.

Applicants have amended claims 1, 17, 31, 32 and 35 to recite that the binding agent has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding agent. Support for this amendment is provided, e.g., on page 45, Table 1 of the specification.

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Applicants have amended claims 2-6 to conform the recitation of "bone morphogenetic" to that of amended claim 1, from which the claims depend.

Applicants have amended claims 32 and 33 to recite "housing" rather than "adapted to house" to more clearly define the invention. Support for this amendment is provided, e.g., on page 9, lines 21-24 of the specification.

Applicants have added claim 37 to recite the device of claim 5 wherein the amount of the OP-1 ranges from approximately 0.125 mg to 10.0 mg. Support for this amendment is provided, e.g., on page 96, lines 8-9 of the specification.

Applicants have added claim 38 to recite the device of claim 37 wherein the amount of the OP-1 is approximately 3.5 mg. Support for this amendment is provided, e.g., on page 96, lines 8-9 of the specification.

None of the amendments adds new matter.

Applicants address the Examiner's rejection below:

35 U.S.C. § 103(a)

Claims 1-5, 7, 8, 11-13 and 31

The Examiner has rejected claims 1-5, 7, 8, 11-13 and 31 under 35 U.S.C. § 103(a) as being obvious over U.S. Patent 5,422,340 ("Ammann"), U.S. Patent 5,597,897 ("Ron") and Bulletin VC-453 ("Bulletin"). The Examiner states that TGF- β is clearly an osteogenic protein, as evidenced by Ammann and that although the specification intends the term "osteogenic proteins" to include members of the family of bone morphogenetic proteins, the specification in no way limits the "osteogenic protein" of the present claims to a BMP subgroup of the TGF- β superfamily of growth factors. The Examiner further states that Figure 4 of the Bulletin indicates that high viscosity grade CMC having a 0.7 degree of substitution has a viscosity within the range of about 10-200 cP at the appropriate concentration. Accordingly, the Examiner concludes that Ron teaches a binding agent having a viscosity of about 10-200 cP and a degree of substitution of 0.65-0.90.

First, applicants respectfully submit that claim 7 was previously canceled in applicants' November 3, 2003 response, rendering the Examiner's rejection with respect to claim 7 moot. Second, applicants have amended claims 1 and 31

(and therefore, claims dependent therefrom) to recite that the binding agent or carboxymethylcellulose has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding agent or carboxymethylcellulose.

Nothing in Ammann, Ron and the Bulletin render the claims as amended obvious. Ammann discloses a bone-inducing formulation comprising TGF- β and TCP and optionally, a polymer for enhancing the consistency of the formulation useful for binding the TGF- β to the TCP to form a smooth, moldable putty or paste. Ron discloses a composition comprising an osteogenic protein selected from BMPs 1-8, a polymer matrix and an osteogenic protein sequestering material including cellulose. Ron discloses that the CMC has a 0.7 degree of substitution and a viscosity of 2480 cP. The Bulletin at Figure 4 discloses the viscosity of various CMCs having a 0.7 degree of substitution at different concentrations. However, nothing in the combination of Ammann, Ron, and the Bulletin teaches or suggests a device comprising a bone morphogenetic protein and a binding agent wherein the binding agent or CMC has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding

agent or CMC. Therefore, applicants request that the Examiner withdraw this obviousness rejection.

Claims 1, 15, 16, 32, 33, 35 and 36

The Examiner has rejected claims 1, 15, 16, 32, 33, 35 and 36 under 35 U.S.C. § 103(a) as being obvious over Ammann and Ron in view of Arnaud E. et al., "Potentiation of transforming growth factor (TGF-beta 1) by natural coral and fibrin in a rabbit cranioplasty model", *Calcif. Tissue Int.*, Vol. 54(6), pp. 493-498 (1994) ("Arnaud") and Turco, S. J. et al., "Intravenous Admixtures", Chapter 85 in *Remington's Pharmaceutical Sciences*, 18th Edition, Mack Pub. Co., Easton, Pennsylvania, p. 1570 (1990) ("Turco"). The Examiner states that TGF- β is clearly an osteogenic protein, as evidenced by Ammann and that although the specification intends the term "osteogenic proteins" to include members of the family of bone morphogenetic proteins, the specification in no way limits the "osteogenic protein" of the present claims to a BMP subgroup of the TGF- β superfamily of growth factors. The Examiner states that Figure 4 of the Bulletin indicates that high viscosity grade CMC having a 0.7 degree of substitution has a viscosity within the range of about 10-200 cP at the appropriate concentration. Accordingly, the Examiner states

that Ron teaches a binding agent having a viscosity of about 10-200 cP and a degree of substitution of 0.65-0.90.

As described above, applicants have amended claim 1 (and therefore, claims dependent therefrom) to recite a device for inducing local bone or cartilage formation wherein the binding agent has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding agent. Similarly, claims 32 and 35 (and therefore, claims dependent therefrom) have been amended to recite a kit for inducing local bone or cartilage formation wherein said binding agent has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding agent.

As discussed above, nothing in the combination of Ammann, Ron and the Bulletin render the claims as amended obvious. And, nothing in Arnaud and Turco in combination with these documents render the claims obvious. Arnaud discloses TGF- β 1 compositions in combination with methylcellulose, fibrin glue and/or natural coral skeleton. Turco discloses intravenous fluids and their components including electrolyte concentration. None of these references, alone or in

combination, discloses a device or kit wherein the binding agent has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding agent. Accordingly, Ammann, Ron, the Bulletin, Arnaud and Turco taken together do not teach or suggest a device or kit as recited in claims 1, 15, 16, 32, 33, 35 and 36. Accordingly, applicants request that the Examiner withdraw this obviousness rejection.

35 U.S.C. § 112, 1st Paragraph

Claims 1, 8, 9, 11-16, 20-22, 32, 33, 35 and 36

The Examiner has rejected claims 1, 8, 9, 11-16, 20-22, 32, 33, 35 and 36 under 35 U.S.C. § 112, first paragraph for lack of written description. Specifically, the Examiner contends that although the recitation of "osteogenic protein" is generally understood to mean a protein which can induce the full cascade of morphogenic events culminating in endochondral bone formation, it describes at best what an "osteogenic protein" does, rather than what it is.

Applicants have amended claims 1, 32 and 35 (and therefore, claims dependent therefrom) to replace the term "osteogenic protein" with "bone morphogenetic protein", thus, obviating the Examiner's rejection.

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35 U.S.C. § 112, 2nd Paragraph

Claims 1-6, 8, 9, 11-25, 31-33, 35 and 36

The Examiner has rejected claims 1-6, 8, 9, 11-25, 31-33, 35 and 36 under 35 U.S.C. § 112, second paragraph, stating that the recitation of "viscosity of about 10-200 cP" is indefinite because viscosity of cellulosic materials depends on the concentration.

Applicants have amended claims 1, 17, 31, 32 and 35 (and therefore, claims dependent therefrom) to recite a device or kit for inducing local bone and cartilage formation wherein the binding agent has a degree of substitution of 0.65-0.90 and a viscosity of about 10-200 cP at a 4% (w/v) concentration of said binding agent, thus, obviating the Examiner's rejection with respect to these claims. Support for this amendment is provided, e.g., at page 45, Table 1 of the specification.

35 U.S.C. § 102(b)

Claims 32, 33, 35 and 36

The Examiner has rejected claims 32, 33, 35 and 36 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 4,353,982 ("Gomez"). The Examiner states that the claims are

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directed to or encompass a kit comprising receptacles and that they do not require that the receptacles contain anything in particular. The Examiner states that the claims only require that the receptacles are adapted to house the recited contents. The Examiner states that Gomez discloses a kit comprising three receptacles and the receptacles are adapted to house the components recited in the present claims in the absence of evidence to the contrary. Applicants traverse.

Applicants disagree that the claims are directed to or encompass a kit comprising receptacles, which do not contain anything in particular. However, to expedite prosecution, applicants have amended claims 32 and 35 (and therefore, claims dependent therefrom) to recite "housing" rather than "adapted to house." Support for this amendment is provided, e.g., on page 9, lines 21-24 of the specification. Gomez discloses a kit comprising containers comprising antibodies. Gomez does not teach a kit for inducing local bone or cartilage formation, comprising receptacles housing the various components recited in the amended claims. Accordingly, applicants respectfully request that the Examiner withdraw this novelty rejection.

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CONCLUSION

In view of the foregoing remarks and amendments, applicants request that the Examiner favorably reconsider this application and allow the claims pending herein. If the Examiner believes that a telephone conference would expedite allowance of this application, he is invited to telephone the undersigned at any time.

Respectfully submitted,



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